



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,557	05/02/2002	Audrey Goddard	GNE.3230R1C39	9770

7590 06/09/2005

AnneMarie Kaiser
Knobbe Martens Olson & Bear
Sixteenth Floor
620 Newport Center Drive
Newport Beach, CA 92660

EXAMINER

BLANCHARD, DAVID J

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 06/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/063,557

Applicant(s)

EATON ET AL.

Examiner

David J. Blanchard

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 March 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 3/22/05; 4/13/05.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Exhibit A.

HL

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 22 March 2005 has been entered.
2. Claim 6 has been canceled.
Claim 1 has been amended.
3. Claims 1-5 are pending and under examination.
4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
5. This Office Action contains New Grounds of Rejections.

Inventorship

6. The request for the deletion of inventors Eaton, Filvaroff, Gerristen and Watanabe is approved and the inventors have been deleted.

Rejections Withdrawn

7. The rejection of claims 1-5 under 35 U.S.C. 103(a) as being unpatentable over Lal et al (WO 00/00610, 1/6/2000, cited previously) in view of Queen et al (US Patent

5,530,101, issued 6/1996) is withdrawn in view of applicants arguments and the fact that Lal et al do not teach the expression of the polypeptide or a function for the protein.

Response to Arguments

8. The rejection of claims 1-5 under 35 U.S.C 101 because the claimed invention is not supported by a substantial asserted utility or a well-established utility is maintained.

The response filed 3/22/2005 has been carefully considered, but is deemed not to be persuasive. Applicant reviews the evidentiary standard regarding the legal presumption of utility. The examiner takes no issue with Applicant's discussion of the evidentiary standard regarding the legal presumption of utility. Applicant argues that the utility need not be proved to a statistical certainty, a reasonable correlation between the evidence and the asserted utility is sufficient and applicant cites numerous case law in support of applicants arguments that for a therapeutic and diagnostic use, utility does not have to be established to an absolute certainty and the evidence need not be direct evidence so long as there is a reasonable correlation between the evidence and the asserted utility. Applicant argues that as set forth in MPEP 2107 II(B)(1) "If applicant has asserted that the claimed invention is useful for any particular practical purpose... and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility." In response to these arguments, the examiner agrees with Applicant's statement that absolute certainty is not the legal standard for utility. However, the rejection does not question the presumption of truth, or credibility, of the asserted utility. The asserted utilities of cancer diagnostics and

Art Unit: 1642

cancer therapeutics for the claimed polypeptides are credible and specific, however, they are not substantial. The data set forth in the specification are preliminary at best because the specification does not teach the expression of the PRO1069 polypeptide nor any particular biological activity of the polypeptide. Applicant summarizes their arguments and the disputed issues involved. Applicant reiterates that Example 18 in the specification shows that mRNA encoding the PRO1069 polypeptide is more highly expressed in normal kidney compared to kidney tumor and applicant asserts that it is well-established in the art that a change in the level of mRNA for a particular protein, generally leads to a corresponding change in the level of the encoded protein and based on the identification of the mRNA encoding the PRO1069 polypeptide under-expressed in tumor tissue compared to normal tissue renders the PRO1069 polypeptide useful as a diagnostic tool for the determination of the presence or absence of tumor. In support, applicant again argues with the declaration of J. Christopher Grimaldi (previously submitted as Exhibit 1) that there is at least a two-fold difference in PRO1069 mRNA between kidney tumor and normal kidney tissue. This has been fully considered, but is not found persuasive. First, it is important to note that the instant specification provides no information regarding PRO1069 polypeptide levels in tumor samples relative to normal samples. Only gene expression data was presented. Therefore, the declaration is insufficient to overcome the rejection of claims 4-9, 11-17 based upon 35 U.S.C. 101 and 112, first paragraph, since it is limited to a discussion of data regarding the gene expression of the PRO1069 cDNA and not gene expression levels and polypeptide levels. Furthermore, the declaration does not provide data such

Art Unit: 1642

that the examiner can independently draw conclusions. There is no evidentiary support to Dr. Grimaldi's statement that if a difference in gene expression is detected, this indicates that the gene and its corresponding polypeptide and antibodies against the polypeptide are useful for diagnostic purposes, to screen samples to differentiate between normal and tumor. Finally, it is noted that the literature cautions researchers from drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. For example, Hu et al (Journal of Proteome Research 2:405-412, 2003, Ids reference 23 filed 3/31/2005) analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column). Hu et al. discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section).

Applicant argues that they have established that the accepted understanding in the art is that there is a direct correlation between mRNA levels and the level of expression of the encoded protein and applicant argues with the previously submitted second declaration of J. Christopher Grimaldi (previously submitted as Exhibit 2), which states that those who work in this field are well aware that in the vast majority of cases, when a gene is over-expressed ...the gene product or polypeptide will also be over-expressed and this same principle applies to gene under-expression. Further, applicant

Art Unit: 1642

argues with the declaration of Dr. Paul Polakis (previously submitted as Exhibit 3) which states that based upon his experience accumulated in more than 20 years of research, that it is his scientific opinion that for human genes, an increased level of mRNA in a tumor cell relative to a normal cell typically correlates to a similar increase of the encoded protein in the tumor cell relative to the normal cell and that based on his experience although reports exist where such a correlation does not exist, such reports are exceptions to a commonly understood general rule that increased mRNA levels are predictive of corresponding increased levels of the encoded protein and applicant cites Alberts [a] (4th ed. 2002; Exhibit 2), Alberts [b] (3rd ed. 1994; Exhibit 1), Lewin and Zhigang for support that mRNA expression correlates with protein expression. The declarations of Dr. Grimaldi and Dr. Polakis and applicant's arguments have been fully considered, but are not found persuasive. Alberts [b] and Lewin actually support the fact that further research would have to be carried out to determine if the polypeptide expression levels track with the expression levels of the corresponding mRNA. Alberts and Lewin show that there are several levels that control gene expression both at the transcriptional (i.e., mRNA synthesis) and the translational (i.e., protein production) levels. Thus, one skilled in the art would not accept that increased mRNA levels directly correlate with the level of the corresponding polypeptide in view of the multitude of controls at the transcriptional and translational levels. With respect to applicant's arguments regarding the art of Zhigang et al, the art of Zhigang et al does show protein expression, however, the experiments were carried out to demonstrate this and as such Zhigang support that one needs to actually determine the expression of the protein to

Art Unit: 1642

be sure of expression. Applicant also argues that Alberts [a] (4th ed. 2002; Exhibit 2). figure 6-3 on page 302 illustrates the general principle that there is a correlation between increased gene expression and increased protein expression. In response to this argument, while increased transcript levels can lead to increased polypeptide levels, there are other regulatory factors that also effect the rate of translation as evidenced by Alberts [b] (Exhibit 1) in Figure 9-72. Additionally, Meric et al (Molecular Cancer Therapeutics, 1:971-979, 2002, Ids reference 17, filed 3/22/2005) teaches that in addition to variations in mRNA sequences that increase or decrease translational efficiency, changes in the expression or availability of components of the translational machinery (i.e., over-expression of eIF4E, eIF4G, eIF-2 α , eIF-4A1, ect...) as well as activation of translation through aberrantly activated signal transduction pathways also effect the rate of translation in cancerous cells. Figure 6-3 of Exhibit 2 (Alberts, 4th ed. 2002) does not account for these other types of controls that exist in cancerous cells. Applicant argues that Meric et al states at page 791, left column that the fundamental principle of molecular therapeutics is to exploit differences in gene expression between cancer cells and normal cells and most efforts have concentrated on identifying differences in gene expression at the level of mRNA, which can be attributable to either DNA amplification or to differences in transcription and applicant concludes that those of skill in the art would not be focusing on differences in gene expression between cancer cells and normal cells if there were no correlation between gene expression and protein expression. First, the statements by Meric appear to have been taken out of context. Meric indicates most efforts have concentrated on gene expression at the mRNA level

Art Unit: 1642

due to the advent of cDNA array technology, which facilitated this type of analysis. Further, Meric et al in agreement with Alberts and Lewin acknowledges that gene expression is quite complicated and is regulated at the level of mRNA stability, mRNA translation and protein stability and Meric goes on to discuss that the components of the translation machinery and signal pathways involved in the activation of translation initiation represent good targets for cancer therapy (see pages 975-976). If it is the accepted understanding in the art that there is a direct correlation between mRNA levels and the level of expression of the encoded polypeptide, there would not be a need to target the translational machinery, unless of course the two are regulated separately.

Further, applicant argues that the statement of Jang et al (cited previously by the examiner) that "further studies are necessary to determine if changes in protein levels track with changes in mRNA levels for metastasis associated genes in murine tumor cells." does not imply that the reason for additional research is needed is because the levels of mRNA and protein were measured and found not to correlate, rather, the statement simply acknowledges that Jang did not attempt to correlate mRNA and protein levels, and thus further research would be required to do so. In response to this argument, the examiner recognizes that the statement by Jang does not mean that mRNA and protein levels were measured and found not to correlate, the point was the acknowledgement by Jang that further research would be required to determine if a correlation between mRNA and protein levels actually exists. Again, if it is established that the accepted understanding in the art that there is a direct correlation between mRNA levels and the level of expression of the encoded protein, Jang et al would not

Art Unit: 1642

state that "further studies are necessary to determine if changes in protein levels track with changes in mRNA levels for metastasis associated genes in murine tumor cells."

Applicant acknowledges that the examiners citations of Vallejo et al, Powell et al, and Fu et al as examples of post-transcriptional regulation of protein levels, they are not inconsistent with applicant's position that mRNA levels correlate, more often than not, with protein levels. In response to this argument, and in agreement with the art of Vallejo et al, Powell et al, Fu et al and Jang et al, Gygi et al (Molecular and Cellular Biology, 19(3):1720-1730, March 1999) states "We found that the correlation between mRNA and protein levels was insufficient to predict protein expression levels from quantitative mRNA data. Indeed, for some genes, while the mRNA levels were of the same value the protein levels varied by more than 20-fold. Conversely, invariant steady-state levels of certain proteins were observed with respective mRNA transcript levels that varied by as much as 30-fold." (see abstract). Also, Haynes et al (1998, Electrophoresis 19:1862-1871, *Id's* reference 10 filed 3/22/2005), who studied more than 80 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between polypeptide and transcript level. For some genes, equivalent mRNA levels translated into protein abundances, which varied more than 50-fold. Haynes et al concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript (p. 1863, second paragraph, and Figure 1). In agreement with Gygi and Haynes, Hanish S. [a] (Nature Reviews, Applied Proteomics Collection, pp. 9-14, March 2005) recently stated "There is a need to profile gene expression at the level of the proteome and to correlate changes in gene-

Art Unit: 1642

expression profiles with changes in proteomic profiles. The two are not always linked- numerous alterations occur in protein levels that are not reflected at the RNA level.”

(see page 12). Further, Hanash [a] teaches that tumors are complex biological systems and no single type of molecular approach fully elucidates tumor behavior, necessitating analysis at multiple levels encompassing genomics and proteomics (see abstract).

Hanash et al [b] (The Pharmacogenomics Journal, 3(6):308-311, 2003) states “However perfected DNA microarrays and their analytical tools become for disease profiling, they will not eliminate a pressing need for other types of profiling technologies that go beyond measuring RNA levels, particularly for disease-related investigations.” (see page 311). According to Hanash et al [b], there is a need to assay protein levels and activities and numerous alterations may occur in proteins that are not reflected in changes at the RNA level (see page 311). Clearly, contrary to applicant’s arguments and as evidenced by the art above, it is not established in the art that the accepted understanding is that there is a direct correlation between mRNA levels and the level of expression of the encoded protein. The literature supports that RNA expression cannot inevitably be correlated with levels of the encoded polypeptide and one skilled in the art would not assume that the levels of RNA are predictive of the levels of the encoded polypeptide given the distinct regulation of transcription and translation as evidenced by Alberts, Lewin, Meric, Jang et al, Vallejo et al, Powell et al, Fu et al, Gygi et al, Haynes et al, Hanash S [a] and Hanash et al [b]. One skilled in the art would do further research to determine whether or not the PRO1069 polypeptide was under-expressed in kidney tumor samples. Such further research requirements make it clear that the

Art Unit: 1642

asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. This situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sup. Ct, 1966), in which the court held that

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field" and "a patent is not a hunting license" "[i]t is not a reward for the search, but compensation for its successful conclusion."

Applicant refers to three additional articles previously submitted by Applicant (Orntoft et al; Exhibit filed 8/16/2004, Hyman et al; Exhibit filed 8/16/2004, and Pollack et al; Exhibit filed 8/16/2004) as providing evidence that gene amplification generally correlates with levels of the encoded polypeptide. Applicant characterizes Orntoft et al as teaching mRNA and protein levels for individual genes located within amplified or deleted chromosomal regions and found that of the 40 proteins analyzed only one showed disagreement between transcript alteration and protein alteration (Orntoft, page 42). This has been fully considered, but is not found to be persuasive. Orntoft appear to have looked at increased DNA content over large regions of chromosomes and comparing that to mRNA and polypeptide levels from the chromosomal region. This approach to investigating gene copy number was termed CGH. Orntoft et al do not appear to look at gene amplification, mRNA levels and polypeptide levels from a single gene at a time. The instant specification reports data regarding amplification of

Art Unit: 1642

individual genes, which may or may not be in a chromosomal region, which is highly amplified. Orntoft et al concentrated on regions of chromosomes with strong gains of chromosomal material containing clusters of genes (page 40). This analysis was not done for PRO1069 in the instant specification. That is, it is not clear whether or not PRO1069 is in a gene cluster in a region of a chromosome that is highly amplified. Therefore, the relevance of Orntoft et al is not clear. Hyman et al used the same CGH approach in their research. Less than half (44%) of highly amplified genes showed mRNA over-expression (abstract). Polypeptide levels were not investigated. Therefore, Hyman et al also do not support utility of the claimed polypeptides. Pollack et al also used CGH technology, concentrating on large chromosome regions showing high amplification (page 12965). Pollack et al did not investigate polypeptide levels. Therefore, Pollack et al also do not support the asserted utility of the claimed invention. Importantly none of the three papers reported that the research was relevant to identifying probes that can be used as cancer diagnostics. The three papers state that the research was relevant to the development of potential cancer therapeutics, but also clearly imply that much further research was needed before such therapeutics were in readily available form. Accordingly, the specifications assertions that the claimed PRO1069 polypeptides have utility in the fields of cancer diagnostics and cancer therapeutics are not substantial.

For these reasons the rejection is maintained.

9. The rejection of claims 1-5 under 35 U.S.C. 112, first paragraph, is maintained. Specifically, since the claimed invention is not supported by a substantial utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

10. The rejection of claims 1-5 under 35 U.S.C. 112, first paragraph, because the claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained.

The response filed 3/22/2005 has been carefully considered, but is deemed not to be persuasive. The response argues that in general differential expression levels of mRNA leads to differential protein expression levels and this is the general understanding in the art and the references cited by the examiner are exceptions to the general rule. Applicant relies on example 18 of the specification, the art of Zhigang and Meric for support and states that the totality of the evidence clearly establishes that those of skill in the art would believe that mRNA levels more likely than not correlate with protein levels. In response to this argument and as discussed above in the utility rejection the art of Alberts, Lewin, Meric, Jang et al, Vallejo et al, Powell et al, Fu et al, Gygi et al, Haynes et al, Hanash S [a] and Hanash et al [b] underscores the unpredictability in the art and the predictability of protein translation and its possible use as a diagnostic are not necessarily contingent on the levels of mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. In view of

Art Unit: 1642

the totality of evidence of record, one of skill in the art could not predictably use the antibodies of the present claims as a diagnostic or therapeutic agent with a reasonable expectation of success.

New Grounds of Rejections

Priority

Applicant claims priority to five previous applications in the preliminary amendment of 09 September 2002. Priority is granted to PCT/US00/23328, filed 24 August 2000, as the disclosure of '328 is identical to the instant disclosure. However, priority is not granted to USSN 09/380,137, PCT/US99/12252 and 60/088,740 since these applications do not disclose the microarray assay upon which applicant relies for utility of the instantly claimed polypeptides. Therefore, the filing date for the purpose of art rejections is deemed to be 24 August 2000. Applicant is reminded that benefit to a prior-filed application requires written description and enablement under the first paragraph of 35 U.S.C. 112.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent,

except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(a) as being anticipated by Lal et al (WO 00/00610, 1/6/2000, cited previously on PTO-892 mailed 4/15/2004).

The claims are drawn to an antibody that specifically binds to the polypeptide of SEQ ID NO:50, wherein the antibody is a monoclonal antibody, an antibody fragment and is labeled.

Lal et al teach a polypeptide (SEQ ID NO:35), which is identical to the instantly claimed polypeptide of SEQ ID NO:50 and antibodies that bind the polypeptide are monoclonal, antibody fragments and labeled (see pages 44-45 and 52-53).

13. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(e) as being anticipated by Walker et al (U.S. Patent 6,277,574 B1, 4/9/1999).

The claims have been described supra.

Walker et al teach a polypeptide (SEQ ID NO:11) that is identical to the polypeptide of SEQ ID NO:50 (see the alignment attached to the back of this Office Action; Exhibit A) and Walker teaches monoclonal antibodies and antibody fragments that specifically bind the polypeptide and the antibodies may be labeled with a therapeutic agent for treating disease in a subject (see column 13).

14. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walker et al (U.S. Patent 6,277,574 B1, 4/9/1999) in view of Queen et al (U.S. Patent 5,530,101, issued 6/96, cited previously on PTO-892 mailed 4/15/2004).

The claims have been described supra. Claim 3 recites wherein the antibody is a humanized antibody.

Walker et al have been described supra. Walker et al does not teach a humanized antibody. This deficiency is made up for in the teachings of Queen et al.

Queen et al teach humanized antibodies for human therapy (see entire document).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a humanized antibody to the polypeptide of Walker et al in view of Queen et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a humanized antibody to the polypeptide of Walker et al in view of Queen et al because Walker et al teach the polypeptide of SEQ ID NO:50 (i.e., SEQ ID NO:11 of Walker et al) is associated with kidney disease and it would be obvious in view of Queen et al who teaches humanized antibodies to humanize the antibody of Walker et al for human therapy.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusions

15. No claim is allowed.

Art Unit: 1642

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to the Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827



JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
6/7/05

Exhibit A

RESULT 1
US-09-289-349-11
; Sequence 11, Application US/09289349
; Patent No. 6277574
; GENERAL INFORMATION:
; APPLICANT: Walker, Michael, G.
; APPLICANT: Volkmuth, Wayne
; APPLICANT: Klinger, Tod, M.
; APPLICANT: Azimzai, Yalda
; APPLICANT: Yue, Henry
; TITLE OF INVENTION: GENES ASSOCIATED WITH DISEASES OF THE KIDNEY
; FILE REFERENCE: PB-0010 US
; CURRENT APPLICATION NUMBER: US/09/289,349
; CURRENT FILING DATE: 1999-04-09
; NUMBER OF SEQ ID NOS: 12
; SOFTWARE: PERL Program
; SEQ ID NO 11
; LENGTH: 89
; TYPE: PRT
; ORGANISM: Homo sapiens
; FEATURE: -
; OTHER INFORMATION: 1900433CD1
US-09-289-349-11

Query Match 100.0%; Score 461; DB 3; Length 89;
Best Local Similarity 100.0%; Pred. No. 1.1e-51;
Matches 89; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MERTVLALLLLAGLTALEANDPFANKDDPFYYDWKNLQLSGLICGGLLAIAAGIAAVLSGK	60
Db	1	MERTVLALLLLAGLTALEANDPFANKDDPFYYDWKNLQLSGLICGGLLAIAAGIAAVLSGK	60
Qy	61	CKYKSSQKQHSVPVEKAIPITPGSATTC	89
Db	61	CKYKSSQKQHSVPVEKAIPITPGSATTC	89